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Canada

CERVICAL CANCER SCREENING PROGRAMS 1982

Report of a Task Force
reconvened by the
Health Services Directorate
Health Services and Promotion Branch

Cervical Cancer Screening Programs 1982

Report of a Task Force reconvened by the Health Services Directorate, Health Services and Promotion Branch

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This is the full report of a summary that appeared in the Oct. 1, 1982 issue of the *Canadian Medical Association Journal.*

FOREWORD

In the light of significant new data, and in response to concerns expressed by national and provincial associations, professionals, and members of the Task Force who had written the 1976 report "Cervical Cancer Screening Programs", the Department of National Health and Welfare reconvened a group of experts to review the subject.

This report is not a statement of federal government policy. It constitutes a part of the information base from which policies may be developed. It is hoped that the report will be a valuable guide to others in planning, setting policy on, and administering clinical and laboratory activities in cervical cancer screening programs in Canada.

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LETTER OF TRANSMITTAL

arry Fry
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tment of National Health and Welfare
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Mr. Fry:

ny privilege to transmit to you the report of the Reconvened Task Force on Cervical r Screening Programs. The original Task Force which was set up by the Conference outy Ministers of Health in 1973, published its report in 1976.

Task Force was reconvened in response to concerns expressed by national and cial associations, professionals, Task Force members, and others, regarding the 1976 on CERVICAL CANCER SCREENING PROGRAMS. These concerns stemmed from cant new data, changing socio-sexual patterns, and wide variations in implementa- f the 1976 recommendations.

982 recommendations deal with frequency of screening; laboratory quality control; llow-up mechanisms. New chapters appear on risk groups; mathematical models of ing; quality control in screening programs; and management of patients with nal smears.

all, the Task Force views as unnecessary the annual screening of women over 35 of age, whose previous smears have been normal. By reducing the frequency of nation in such women, and deploying resources to concentrate on women at risk tly not being screened, Canadian cervical cancer screening programs could become effective at no additional cost.

n recommendations - such as those dealing with the development of efficient tories and central registries - require implementation by governments. However, e of frequency of examination will only be implemented if the health professions, e public at large, are persuaded that this is a reasonable thing to do.

all the members of the Task Force for their excellent contributions to the work of sk Force with its report. Thanks are also due to those institutions which made e their devoting so much time to the task. Special thanks are extended to D. Gellman for acting as Editor of the report.

k those colleagues in clinical and academic domains, who responded to the Task s survey for comments on the first report.

I acknowledge the considerable assistance given to the Task Force by the officials Department of National Health and Welfare, especially the great contribution of ssirer of the Health Services Directorate, in her capacity as Co-ordinator of the orce.

Yours sincerely,

R.J. Walton, M.B., Ch. B., F.R.C.R.,
Chairman,
Reconvened Task Force on
Cervical Cancer Screening Programs

Terms of Reference

1. To review the conclusions and recommendations of the 1976 report on Cervical Cancer Screening Programs in the light of any new data which might support or modify the conclusions on which the original recommendations were based.
2. To confirm or change the original conclusions and recommendations, and to arrive at new conclusions and make new recommendations, if appropriate.

Schedule of Meetings

January 11, 1980	Ottawa
March 24 and 25, 1980	Vancouver
May 11, 12 and 13, 1980	Quebec
September 3 and 4, 1980	Toronto
November 20 and 21, 1980	Edmonton
February 26 and 27, 1981	Ottawa
June 29 and 30, 1981	Kingston

Members of Reconvened Task Force

Dr. R.J. Walton (Chairman)	Consultant Manitoba Cancer Treatment and Research Foundation Winnipeg, Manitoba and Member, Honorary Medical Staff Formerly Vice President, Medical Health Sciences Centre Winnipeg, Manitoba
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Eve Kassirer, M.A. (Co-ordinator of Task Force)	Medical Sociologist Institutional and Professional Services Division Health Services Directorate Health Services and Promotion Branch Department of National Health and Welfare Ottawa, Ontario

The Task Force acknowledges resource assistance from:

Dr. Eve Shulman
Epidemiologist
Health Assessment Division
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Ottawa, Ontario.

removal of the cervical epithelium; and
(b) the group *at risk*, which comprises all other women.

13. In general, Canadian women aged 35 years or more who have regularly participated in screening programs and who have had at least two screening tests without significant atypia, should require screening no more often than every five years.

14. Canadian women under 35 are probably now more active sexually than earlier generations and increasingly tend to have more than one partner; annual screening is appropriate for this age group.

15. There is as yet no evidence that oral contraceptives, of themselves, increase the risk of developing cancer of the cervix.

16. The malignant diseases which most frequently affect women in Canada — cancer of the breast, large bowel, ovary, lung and endometrium — occur in women 20 to 30 years older than those on whom a screening program for carcinoma of the cervix and its precursors should concentrate. Thus, although opportunities created by screening or medical examinations for these diseases should be utilised in taking cervical smears which are due, the frequency of cervical smears should not be affected by examinations for them.

17. There is no evidence that a cervical cytologic screening program will reduce mortality from other gynaecologic conditions, other than carcinoma of the cervix.

18. There is no evidence that annual pelvic examinations of asymptomatic womem, per se, will lead to reduction in mortality from cancer of the endometrium or ovary.

19. Colposcopy is valuable for assessing the significance of abnormalities found in a cervical smear, particularly in young women. It imposes a large degree of responsibility for accurate evaluation on the colposcopist.

20. Primary responsibility to enter and continue in a cervical cancer screening program lies with individual women. Physicians, other health professionals, and government public health agencies all have a role in education and in ensuring that screening programs are available, are of adequate quality, and that cervical smears are obtained at an appropriate frequency.

Recommendations*

he recommendations of the Task Force should be taken
a whole. It is inappropriate to establish the recom-
ended screening frequencies as formal policy in the
sence of established systems to monitor the frequen-
es and to issue reminders to attend at the recommend-
l intervals in the absence of proper quality control
stems.

On the basis of its conclusions the members of the Task
orce recommend the following:

I. Health authorities should encourage and support
he development of cytologic screening programs designed
o detect the precursors of clinical carcinoma of the
ervix.

II. Women who have had sexual intercourse should generally be advised to have screening annually between the ages of 18 and 35 years and thereafter every five years until age 60.

III. Women over the age of 60 who have had repeated satisfactory smears without significant atypia may be dropped from a screening program for squamous cell carcinoma of the cervix.

IV. High priority should be given to encouraging women at risk who have never had a cervical cytology examination to have one and to enter a screening program.

V. The recommended screening frequencies apply only to women whose smears show epithelial cell atypia. Once such changes are detected schedules for repeat examinations should be dictated by the requirements for surveillance, diagnosis, treatment and follow-up.

VI. Appropriate means should be employed to inform women of their degree of risk of carcinoma of the cervix. However, no attempt should be made to categorize omen at high risk on a group basis.

VII. Women over 35 years of age whose contact with
e health care system is through venereal disease clinics
penal institutions and who, in their own judgement
that of their physicians, are at high risk should not
discouraged from having smears more frequently than
ery five years if they request them.

VIII. Provincial mechanisms that establish young omen's independent responsibility for health insurance rposes (usually at or about the age of 19 years) should used to remind women that if they are sexually active ey should have a cervical smear if they have not already one so.

IX. Individual screening examinations for various iseases should be promoted on their own merits and performed at the most cost-effective frequency. When two or more screening examinations are being offered, each on its own merits, to the same population group cost-effective considerations may require a change in timing for some of them.

X. Colposcopic examination should not be used as a screening method: it is an important diagnostic tool for localizing and assessing premalignant disease and early invasive carcinoma of the cervix in women with abnormal cervical smears. Colposcopy should be performed only by gynecologists with adequate training and experience in the technique. They should work in a clinical setting that provides a continuing source of abnormal material so that their expertise can be maintained and enhanced.

XI. To function most efficiently within a mass screening program a laboratory should process a sufficient number of cases† annually to require staffing by a minimum of three qualified and experienced cytotechnologists, supervised by a cytopathologist, and adequate clerical and technical support staff.

XII. The jurisdiction responsible for such screening programs should ensure that appropriate mechanisms for quality control have been established and are functioning satisfactorily.

XIII. Uniform terminology, such as that recommended in this report, should be used for reporting smears and biopsies and for recording data in cancer registries so as to assist in the exchange of information from one laboratory to another and to ensure that the various provincial registries are provided with data that are reported in a uniform manner.

XIV. All mass screening programs should have follow-up systems to ensure that:

(a) People with normal test results are recalled at regular intervals for repeat testing according to the guidelines of the program.
(b) Action is taken following the discovery of an abnormality.
(c) Long-term follow-up is provided for patients who have received treatment following the diagnosis of an abnormality.

Such a system can only be effected through a central registry. Provincial registries should establish compatible data-processing systems so that interprovincial communication and comparisons will be possible.

*Some of the following recommendations are unchanged from the 1976 Task Force report. Readers are referred to that report for the rationales.

†Although in the 1976 report 25 000 smears was considered a "sufficient number" (on the basis of efficiency, not proficiency), this number is deleted in the 1982 report. Disagreement with the deletion was registered by one Task Force member, Dr. A.B. Miller.

XV. Provincial licensing bodies should ensure that provincial medical acts and regulations permit physicians to remind their patients when it is time for repeat cervical cytology examinations — or indeed, any other recognized preventive medical procedure.

XVI. Departments and ministers of health should consult with the appropriate bodies in their jurisdictions with a view to selecting the best mechanisms to establish functional registries of all cervical cytology examinations as soon as possible.

XVII. The Deputy Minister of National Health and Welfare should make available the resources of the Department of National Health and Welfare to coordinate the establishment of provincial cervical cytology registries and thus facilitate the exchange of data and the transfer of records when women move from one province or region to another.

Chapter I: Introduction

The report of a Task Force on Cervical Cancer Screening Programs, appointed by the Conference of Deputy Ministers of Health of Canada-which came to be known as the Walton Report — was published in 1976[1]. Although there were some specific criticisms, in general the report was very well received. It stimulated reassessment of current patterns of practice, which was a prime motive of the Deputy Ministers in convening the Task Force.

The 1976 Task Force found that the evidence available supported the conclusion that cervical cytology as practised in Canada had contributed to the declining mortality from carcinoma of the cervix. It recommended that health authorities support the development of screening programs for cervical cancer and that all women should be actively encouraged to participate. The Task Force made recommendations concerning quality control and efficiency in cytology laboratories, on follow-up mechanisms, including the requirement for provincial registries, and on uniform terminology. Perhaps the most controversial conclusion was that the customary "annual" cervical smear was not necesary for the majority of women. The Task Force was criticized for recommending that women who were not at "high risk" (which was defined in general terms), and whose initial two smears (and all subsequent smears) in a properly controlled screening program were satisfactory and without significant atypia, should follow a screening schedule of once every three years to age 35 and then once every five years to age 60. The recommendations concerning size of laboratories and the establishment of registries were also criticized.[2]

Although there was general acceptance of the 1976 Task Force report by the Canadian provinces when it first appeared,[3] implementation has varied widely from province to province depending on finances, priorities, and convictions.[2] Change has proceeded slowly and in a piecemeal fashion. Of particular concern is the fact that only Nova Scotia, Newfoundland and British Columbia have province-wide registries, which were regarded as prerequisites if screening periodicity were to be reduced.

Since the 1976 report was published, new data have become available, providing fresh insights into questions such as the following. What socio-sexual patterns of female and male behaviour precede dysplasia? Which women are at risk? How can at risk women be more precisely classified? What data exist on "high risk" males? What proportion of pre-invasive cancerous lesions regresses? Does the rate of regression vary with age? Who should be responsible for prevention, for the promotion of the cervical smear for at-risk women who seek health care for other reasons, for the communication of relevant socio-sexual knowledge, and for ensuring that women follow appropriate screening schedules? What assessment has there been of the proficiency of existing screening programs? What mechanisms should there be to ensure appropriate action following the discovery of cytologic abnormalities? To what degree does the lack of national consensus on diagnostic criteria, terminology and interpretation distort reported incidence rates and affect treatment? What is the role of colposcopy? How should cost-benefit and cost-effectiveness considerations contribute to decisions on screening programs?

In the light of the new data and in keeping with scientific custom, in January 1980 the Department of National Health and Welfare reconvened a Task Force with minimal changes in membership from that which produced the first report. The mandate of the reconvened Task Force was to review the 1976 recommendations and their implementation in the light of the additional data. The specific Terms of Reference were:

1. To review the conclusions and recommendations of the 1976 report on Cervical Cancer Screening Programs in the light of any new data which might support or modify the conclusions on which the original recommendations were based.
2. To confirm or change the original conclusions and recommendations, and to arrive at new conclusions and make new recommendations, if appropriate.

The present document constitutes the Task Force's 1982 state-of-the-art report. It is based on an examination of data collected from national and international literature and published and unpublished Canadian documents*, and reflects the response of the professional community† to requests by the Task Force for comment on the conceptual and practical aspects of the first report. This report is intended to be read in conjunction with the 1976 report.[1] However, for the sake of clarity, the Conclusions and Recommendations presented here, are integrated and complete.

*Mortality data from Statistics Canada *(Causes of Death,* cat no 84-203) and unpublished tabulations of the British Columbia Central Cytology Registry: incidence data from Statistics Canada (*Cancer in Canada,* cat no 82-207) and the British Columbia Central Cytology Registry; screening coverage data from the Canadian Society of Cytology (unpublished data from a 1980 survey); and data relative to quality control in cytologic screening programs from the Ontario Laboratory Proficiency Testing Program (collected from 1977 to 1981).

†Responses came from university departments of pathology, obstetrics and gynaecology, and family and community medicine; cancer foundations and institutes; and provincial medical associations.

Chapter II: Epidemiology

Since 1976 there has been no reason to challenge the implied conclusion of the Task Force on the etiology of squamous cell carcinoma of the Cervix: namely, that the causes are associated with sexual activity. The most important risk factors in women are generally regarded as being early age at first intercourse, and multiple sexual partners. However, one recent study has suggested that early age at first intercourse does not provide additional characterization of high risk once account is taken of number of sexual partners.[4] If confirmed, this would suggest that the adolescent cervical epithelium may not be specially susceptible to the as yet unidentified etiologic agent or agents.

Because of public concern generated by the information that the factors that cause cancer of the cervix are sexually transmitted, and the dangers of "labelling" patients in this way, it is appropriate to point out that not all patients with clinical invasive disease, or its precursors, have necessarily been "promiscuous" at some time in their lives. The role of the "high risk" male has been emphasized in a number of studies.[5] A woman may develop dysplasia or carcinoma of the cervix even if she has had only one sexual partner in her lifetime; the etiologic agents, whether it be infection or some abnormality of semen or sperm, may have been transmitted to her by that partner.

The epidemiological evidence now available suggests that although herpes simplex virus Type II (HSV II) is not essential for the causation of cancer of the cervix, it may, particularly in high risk geographic areas, lead to pre-malignant change in the cervical epithelial cells in a large majority of cases.[5] However, this knowledge has not yet been translated into the provision of a biological marker which could aid in the identification of women at high risk. Work by Aurelian et al[6] suggests that such a pre-screening tool may eventually become available.

Many authors have described elevated antibody levels to HSV II in patients with carcinoma of the cervix and, recently, in patients with in situ carcinoma.[7] This evidence is circumstantial, but direct evidence of the presence of HSV II RNA in cervical neoplasms has also been found.[8] The technique used is referred to as a viral probe. Tissue from cervical cancer is frozen and sections are placed on a slide and hybridized to in-vitro I^{125}labelled HSV II DNA. After washing and autoradiography, the grains are counted and the number compared to the normal background count.

In a recent study by Wilkie et al,[9] from Glasgow, HSV II RNA was detected in 23 out of 29 in situ cancers, 20 out of 30 squamous cell carcinomas, 1 out of 10 adenocarcinomas and 2 out of 23 normal cervices. This work appears to be reproducible. Thus, there is now direct evidence that HSV II RNA is present in a high proportion of cervical cancers. Techniques are now being developed to discover what part of the viral genome is present in the cells and whether some specific portion of the virus must be present in order for malignant transformation to be induced.

Studies in the last few years have suggested a possible etiologic role for cigarette smoking.[10,11] As most cigarette-associated cancers are of epithelial cell origin, and many are of squamoua type, it is not inconceivable that a carcinogen from cigarette smoke may be of relevance. Recent analyses of data both on cigarette smoking and on variables related to sexual activity suggest that the association could be casual (for example, see Clarke et al [11a]).

There is as yet no evidence that oral contraceptives of themselves increase the risk of developing cervical cancer.

One question relevant to understanding the natural history is whether women with dysplasia or carcinoma in situ have the same distribution of risk factors as those with clinical invasive carcinoma of the cervix. A study by Thomas[12] showed that patients with dysplasia did not differ from population controls in the presence of established risk factors for cancer of the cervix, but that patients with carcinoma in situ did differ. Only patients with severe dysplasia were epidemiologically similar to those with carcinoma in situ and with invasive cancer. Berget[13] also found that women with dysplasia did not have the epidemiologic characteristics of women with carcinoma in situ and invasive carcinoma, and a similar conclusion was reached by Terris, Wilson and Nelson[14] who stated that "cervical dysplasia fails to behave like invasive cancer in any of (the) crucial aspects of cervical cancer epidemiology". Harris et al[4] reached a different conclusion: they found little difference in the expression of risk factors in patients with invasive cancer, carcinoma in situ or dysplasia. They commented that part of the explanation for the different conclusions from findings in different geographical areas may be due to discrepancies in pathological interpretation and nomenclature.

Chapter III: Natural history

In the 1976 report, the Task Force evaluated cross-sectional data from the British Columbia Screening Program to develop a new interpretation that suggested a somewhat longer natural history of carcinoma in situ than had been suspected previously. This interpretation was dependent on an assumption of the progressive nature of the natural history. The Task Force also commented on "studies demonstrating disparity between the predictions of theoretical models and clinical observations of in situ carcinoma, particularly in the later age groups.[15] The cohort study in British Columbia has the potential for resolving this disagreement."

The dilemma in interpretation was well illustrated by Knox[16] who showed, using a mathematical modelling approach with computer simulation, the substantially different impact of screening policies depending on whether one postulated a purely progressive or a "dynamic" natural history. The "dynamic" natural history modelled by Knox involved two components; (1) the possibility that some cases of carcinoma is situ as well as of dysplasia regress, and (2) the possibility that some patients who develop invasive cancer do so after so short a natural history that any reasonable screening program would miss the preceding stages of dysplasia or carcinoma in situ. The reason for postulating the second group is largely theoretical. If some cases regress, and if some persist unchanged without progression, presently derived estimates of mean duration of dysplasia and carcinoma in situ must encompass some cases with rapid progression to clinically invasive cancer. Many of these, of necessity, will occur in younger women, a fact which has to be considered in relation to the efficacy of screening at different ages.

One of the major unanswered questions is the extent to which cases of dysplasia progress. Current approaches to their identification and management are dependent on the assumption that a sufficient proportion do so to justify their treatment. Some studies in progress may help to clarify this issue. The findings from the British Columbia Cohort Study[17] indicate that regression is part of the natural history of carcinoma in situ, especially in younger women. Whether or not an appreciable proportion of women with dysplasia or carcinoma in situ progress rapidly is not apparent from the data, largely because of the short follow-up period for the majority of the women in the study. Fidler et al[18] reported 64 cases of clinical invasive carcinoma occurring in screened women during the years 1961-66, a crude rate of 4.5 per 1000 screened. In reviewing the cytological smears of these cases, 36 were found to have had abnormal cells, which had not been reported originally. In the remaining 28, the time interval from the last negative smear to the diagnosis of clinical invasive carcinoma ranged from 1 to 10 years, with 15 having an interval of less than 4 years. At that time, therefore, it seemed that only a small proportion of cases progressed rapidly. Recently, however, there has been anecdotal evidence to suggest that a greater number of rapidly progressive cases may be occurring, especially in younger women.[19]

In a presentation to the NIH Consensus Development Conference on Screening for Cancer of the Cervix, Miller[20] pointed out that if regression of dysplasia or carcinoma in situ occurs, then the extent to which it is observed is an underestimate of the extent to which it actually occurs. On the one hand identified abnormalities might not progress. On the other hand, individuals who happen to be going through a phase of regression, and thus no abnormality at the time of examination, may progress subsequently. This would tend to increase the need for more frequent smears, whereas a purely static or progressive natural history would substantially reduce the requirements, particularly if it were possible to predict that most abnormalities would have occurred by a certain age. Thus, there are two conflicting requirements: first, the need to ensure that too may smears are not done, since these might detect disease which would not have progressed; second, the need to ensure that important progressive disease does nor slip through the screening net.

Chapter IV: Efficacy of screening programs

Incidence of cancer of the cervix in Canada

In the 1976 Task Force report it was concluded that "it is not possible to either prove or disprove the hypothesis that part, possibly a major part, of the observed falls in the incidence of carcinoma of the cervix is due to screening". The only province in which a possible acceleration in the rate of decline due to the screening programs was actually observed was Saskatchewan. However, as pointed out by Miller[21] this impression was not reinforced by later data.

The reconvened Task Force has therefore carefully reviewed the available data on incidence of cancer of the cervix from the Canadian registries. Data are available to 1971 for Ontario, to 1979 for Alberta, Saskatchewan and Manitoba and to 1977 for the rest of the country. For each province with data available to 1977, it is apparent that the rate of decline in incidence in women aged less than 65 has slowed. Indeed, in some provinces there is an indication that there may have been a recent increase in incidence in women aged 20-34 and 35-64. Examples of these trends are presented for Alberta and Manitoba in Fig. 1 and 2. The registered incidence of in situ carcinoma of the cervix at ages 20 or more is also shown: it is apparent that it has increased in these two provinces in recent years. This is particularly so in younger women.

In the 1976 report, the Task Force warned of the difficulties in interpreting incidence data from cancer registries. A cancer registry may not distinguish cases diagnosed on screening from those that present clinically, and, in addition, cases of in situ carcinoma may be registered as invasive if the pathology reports on which registrations are based are not sufficiently specific. Although recent increases in reported incidence of carcinoma in situ could be partly due to such artifacts, it is difficult to explain all changes on such a basis, especially in well-screened areas such as British Columbia, where the incidence of abnormalities discovered on screening would be expected to stabilize rather than rise. An additional factor has entered the picture with the introduction of colposcopy: inexperienced colposcopists may take extremely small biopsies, thus rendering the pathologist's interpretation more difficult.

In British Columbia, the provincial laboratory maintains a special register of new cases of carcinoma of the cervix. Detailed comparison of those cases coded as in-

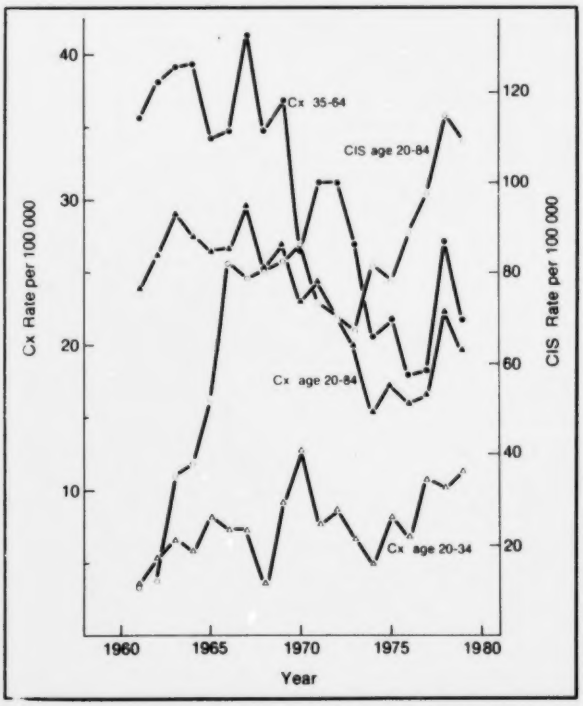

FIG. 1. — Incidence of cancer of the cervix (Cx) and of carcinoma in situ of the cervix (CIS) in Alberta, 1961 to 1979, age standardized rates per 100 000.

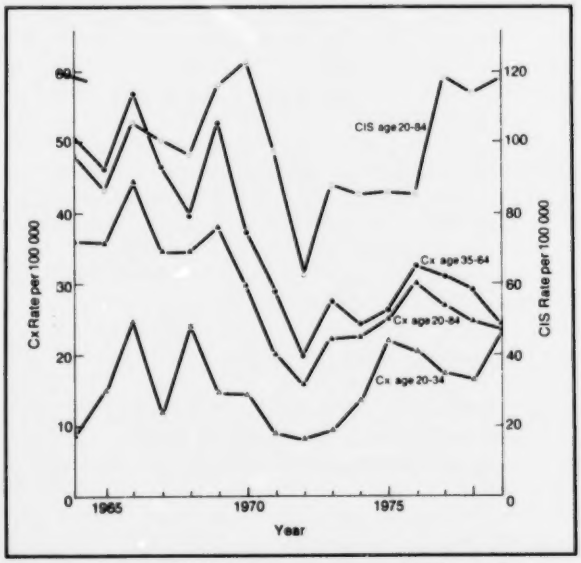

FIG. 2. — Incidence of cancer of the cervix (Cx) and of carcinoma in situ of the cervix (CIS) in Manitoba, 1964 to 1979, age standardized rates per 100 000.

vasive carcinoma of the cervix in the provincial cancer registry with those in the special register is thus possible. In 1975, the provincial registry coded 170 cases as invasive cancer of the cervix (ICD 180). According to the special registry 2 of these were duplicates, 5 cancer of other sites, 51 (30%) were carcinoma in situ, 2 dysplasia and 3 had negative pathological findings. Thus only 107 (63%) were correctly coded in the provincial cancer registry. Even of these, 35 (21% of the total coded) had micro-foci or occult carcinoma, i.e. they were asymptomatic cases diagnosed as a result of screening.

In Fig. 3, the trends of clinical invasive carcinoma in British Columbia as recorded in the special register are given. There was a substantial fall in incidence until 1972. Since then, the rate of fall in women aged 20 to 84 has slowed, and there is a suggestion of a plateau in the rates in women under 64. Unfortunately, as noted in the 1976 report, the provincial cytology laboratory commenced the registry from which these data are drawn only in 1955. Hence data are not available from a baseline period during which no screening was occurring.

The Task Force concludes that currently available data in Canada show that the rate of fall in incidence in all provinces in Canada reported in 1976 has slowed, at least in women under the age of 65, almost universally. In the light of the known risk factors and the change in the prevalence of these risk factors in young women in Canada, this is perhaps not surprising.

It is possible that, were it not for the screening programs in Canada, the registered incidence of invasive cancer would actually have risen. The rising registrations of in situ cancer might be regarded as supporting evidence for this possibility. Reports of advanced squamous cancer of the cervix in screened younger women[19] also support this possibility. If, in the absence of screening, the incidence of invasive cancer were now rising, it might be anticipated that there would also be a rise in the absolute number (though not necessarily in the proportion) of those with rapidly progressive disease not likely to be detected by screening in time to benefit by treatment. In the presence of an effective screening program an increase in the number of such cases will be particularly noticeable because the *proportion* will be much greater. Somewhat paradoxically therefore, the reports of recent increases in the incidence of invasive and in situ cancer do *not* necessarily indicate that the screening programs are ineffective in preventing a large majority of cases from progressing. A further period of observation will be necessary in order to be certain that the rise in registrations of in situ carcinoma will not be followed by a large rise in the incidence of invasive carcinoma.

2. Case-control study in Ontario

Although routinely collected incidence data are unable to provide an answer to the question posed, — i.e. what is the contribution of cytology screening programs to the reduction in the incidence of invasive carcinoma of the cervix that has been observed? — a case-control study based on patients from the County of York, Ontario, treated at the Princess Margaret Hospital during 1973-76, with five controls per case, matched on age and drawn from the same neighbourhood does provide substantial support for the effectiveness of the programs.[22] The multiple controls provided indirect matching on socioeconomic status and gave the investigators the ability to control for a number of possible confounding variables. Subjects who gave no history of having had a cervical smear in the previous five years had a relative risk of approximately three-fold compared to those who had had a smear. This order of risk persisted in those in whom it was possible to obtain confirmation of the cervical smear history from family physicians. Thus we may conclude that a cervical smear within the previous five years will reduce the risk of invasive cancer of the cervix approximately three-fold. It may be noted that this study does not provide support for or refutation of the view that screening for cancer of the cervix will abolish invasive cancer. Nevertheless the expected reduction in incidence, if extended across the whole country, would be impressive and thus it seems probable that screening has contributed to the reduction of incidence seen up to 1975/76. The *extent* of the contribution of screening to this reduction cannot be computed from the study as the controls were matched to the cases and were nor representative of the general population.

One further aspect of this study is relevant to the application of cervical cytology. Only 44% of the cases had been screened in the five years before the diagnosis of carcinoma of the cervix, compared to 63% of the controls. Although this was partly due to the fact that a smaller proportion of the cases (73%) than of the control (88%) had visited a physician in this period, 32% of the cases had had at least one visit to a physician in the five years before the diagnosis of invasive cancer without the opportunity being taken to obtain a cervical smear.

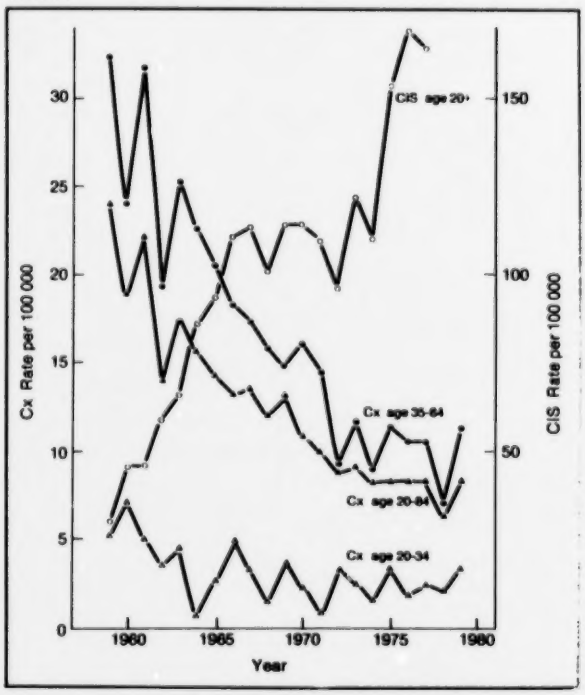

FIG. 3. — Incidence of clinical invasive squamous cell cancer of the cervix (Cx) and of carcinoma in situ (CIS) in British Columbia, 1959 to 1979, age standardized rates per 100 000.

3. Mortality from cancer of the cervix in Canada*

In 1976, the Task Force relied largely on the results of an analysis by Miller, Lindsay and Hill[23] in concluding that:

(a) Cytologic screening programs are becoming effective in reducing mortality from carcinoma of the cervix.
(b) The extent of reduction in mortality is directly related to the proportion of the population that has been screened.

Most commentators, for example the participants in the International Union against Cancer (UICC) Workshop on Screening in Cancer[24], found the analysis of Miller, Lindsay and Hill[23] and the conclusions of the Task Force to be acceptable, although they were challenged by Green,[25] and by Gardner and Lyon,[26] who, from an analysis of US data, reached a different conclusion on the effects of screening in that country.

Canadian data up to 1976, at the provincial level, have recently been evaluated by Miller, Visentin and Howe.[27] The primary purpose was to incorporate data on hysterectomies from 1969 to 1976. Using a number of different extrapolations of the hysterectomy data it was possible to evaluate trends in mortality in Canada at the provincial level based on "uteri at risk", as distinct from "women at risk", in relation to screening indices derived from national surveys with data up to 1971. The analysis showed that the numbers of hysterectomies performed had little impact on the fall in mortality certified due to cancer of the cervix or to all uterine cancer. Further, re-evaluation of the fall in mortality between 1960-62 and 1970-72 in relation to the intensity of screening showed that the hysterectomies performed had little impact on the correlation reported previously.

When the analysis was extended to 1974-76 the correlation between changes in screening index and reduction in mortality disappeared. After pointing out the limitations of correlational analysis which might make it an insufficiently powerful tool to detect small non-linear changes in mortality resulting from increases in screening, Miller, Visentin and Howe[27] suggested several possible explanations for their finding. They regarded as most plausible the explanation that once the population screening index reaches a certain level, further increases lead only to a marginal further reduction in mortality. This might reflect the fact that, in most programs, increase in numbers of examinations largely reflects repeat examinations of the same women rather than initial examinations of previously unscreened women. Yet it is the unscreened women who tend to be at highest risk and in whom most of the mortality from the disease occurs. If they could be included in a program, further reduction in mortality might be achieved.

In Finland, where mass screening is organised on a four-yearly basis, it has been estimated that about 20% of frankly invasive cases have a preinvasive stage shorter than the interval screenings.[28] Although, as pointed out by Miller,[21] part of this "escape from curability" could have been due to false negative smears on first examination, the evidence from Finland, combined with data on attendance rates, enabled Hakama[28] to estimate that not more than a 60% reduction in the incidence of frankly invasive cancer might be possible, a prediction that was verified by the observed trends in cervical cancer. Hence in Canada, within the context of the screening program as applied up to 1976, further reductions in mortality could possibly not have been expected.

Other possible explanations for the disappearance of the association between intensity of screening and reductions in mortality in Canada include an increase in mortality due to changes in the incidence of the disease, especially in the young and the occurrence of preinvasive stages which are less influenced by screening than had been thought to be the case.

It is not possible, on the basis of the evidence presently available, to distinguish between these various explanations. All may contribute. However, the members of the Task Force believe that the results of the analysis of Miller, Visentin and Howe[27] cannot be used to justify any relaxation in the endeavours to control cancer of the cervix through screening using cervical cytology. On the contrary, they emphasize the need to ensure that screening programs are conducted with greater emphasis on screening those at risk women who have never been screened, and the need for good quality control both in the taking of samples and in the functioning of cytology laboratories.

The trends in mortality for ages 20-34, 35-64 and 20-84 (standardized for age, but without correction for hysterectomies performed) for Canada as a whole from 1952-80 are shown in Fig. 4. These data are presented for "malignant neoplasm of cervix uteri" and "other malignant neoplasms of the uterus" combined because of the reducing proportion coded as "uterus unspecified". Other data suggest that the contribution of cancer of the endometrium to total uterine cancer mortality under the age of 65 is very small, and almost stable. It appears from Fig. 4 that the reduction in mortality continues. In British Columbia, the special register maintained by the provincial cytology laboratory carefully evaluates each death certified due to cancer of the cervix and eliminates those not due to squamous cell cancer. Fig. 5 shows the trends from 1959-79 of the resulting mortality rates.

Table I provides information on mortality from carcinoma of the uterus (carcinoma of the cervix, corpus uteri and uterus unspecified combined) of women aged 35 to 64 at the provincial level for 1957-59, 1967-69, and 1977-79. It is apparent that mortality has continued to decline in each province but that the east-west differential, with higher mortality in the east of the country compared with the west, still persists.

Table II gives the mortality for each individual site for 1977-79. Unfortunately, the discrepancy between provinces in the proportion of the total certified to "uterus unspecified", noted in our 1976 report, persists. This makes it difficult to determine the extent to which there is true variation between the provinces in the mortality due to cancer of the corpus uteri. However, these data suggest that the extent of variation of mortality due to cancer at this site is probably less than that due to cancer

* The conclusions of the 1976 report were based on mortality data available to 1972. At the time of the preparation of this report, summary data were available for Canada as a whole to 1980.

of the cervix and that the contribution of mortality from cancer of the corpus to the total is relatively small. Thus most of the major interprovincial differences at these ages are probably due to mortality from cancer of the cervix.

4. Data on efficacy of screening from other countries

Since 1976, new reports on the efficacy of screening for cancer of the cervix have largely appeared from Europe. In Britain, McGregor and Teper[29] continue to report reduced mortality in Aberdeen compared to other areas of the United Kingdom. Yule[30] however, has commented on the increasing mortality from cancer of the cervix in women aged less than 35 in England and Wales.

In the Nordic countries, reductions in mortality have been reported from Iceland[31] and Finland.[32] Perhaps the most convincing evidence of the efficacy of screening programs in these countries comes from a comparison of trends in incidence between Norway and Denmark, Sweden, Finland and Iceland.[33] Only Norway has so far failed to introduce a population screening program for cancer of the cervix, and no reduction in incidence has been noted there. Each of the other Nordic countries has introduced population screening programs and all show a reduction in incidence. Previously Denmark had a higher incidence of cancer of the cervix than the other four Nordic countries, which were all similar. This differential was believed to be due to a corresponding difference in the prevalence of risk factors for cancer of the cervix in the population. Norway, without a population screening program, now has the same high incidence that existed in Denmark before screening was introduced there.

Table I—Mortality* from carcinoma of the uterus (ICD** 180, 182.0 and 182.9), Canadian provinces

Province	Mortality* 1957-59	1967-69	1977-79
Newfoundland	36.4	23.5	18.4
Prince Edward Island	28.8	24.3	19.7
Nova Scotia	32.8	25.8	16.3
New Brunswick	25.2	21.8	11.6
Quebec	33.0	21.3	11.0
Ontario	23.7	17.2	11.4
Manitoba	21.5	11.6	9.3
Saskatchewan	12.3	12.0	7.9
Alberta	20.2	11.8	9.4
British Columbia	21.8	14.7	11.3

*Age standardized rates per 100 000 women aged 35-64 years.
**International Classification of Diseases (ICD) 8th revision.

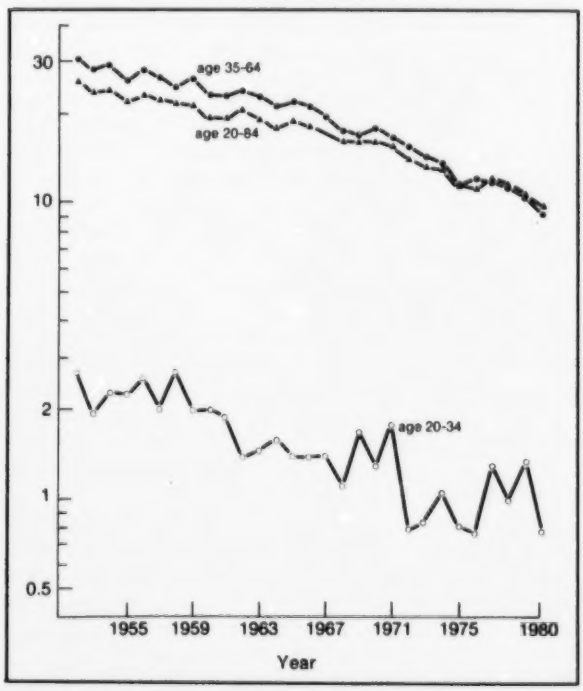

FIG. 4. — Mortality from cancer of the uterus (ICD 180 plus 182) Canada, 1952 to 1980, age standardized rates per 100 000.

Table II—Mortality* from carcinoma of the cervix uteri (ICD** 180), corpus uteri (ICD** 182.0) and uterus, unspecified (ICD** 182.9), Canadian provinces, 1977–79

Province	Mortality* Cervix	Corpus	Uterus unspecified
Newfoundland	14.0	2.2	2.2
Prince Edward Island	12.6	1.6	5.5
Nova Scotia	13.7	2.1	0.5
New Brunswick	7.4	3.6	0.6
Quebec	6.1	2.2	2.7
Ontario	7.5	3.4	0.5
Manitoba	5.6	2.2	1.5
Saskatchewan	5.2	0.6	2.1
Alberta	6.3	1.0	2.1
British Columbia	6.6	3.3	1.4

*Age standardized rates per 100 000 women aged 35 to 64 years.
**ICD 8th revision.

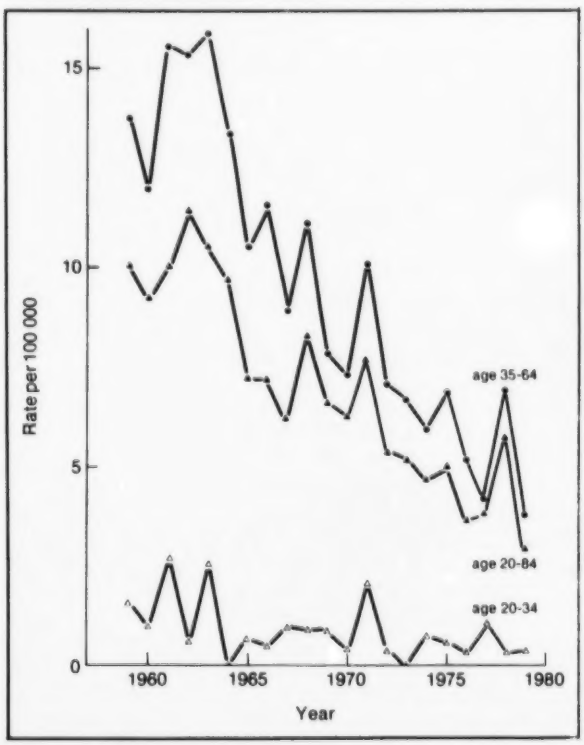

FIG. 5. — Mortality from squamous cell cancer of the cervix, British Columbia, 1959 to 1979, age standardized rates per 100 000.

Chapter V: Risk groups

After the publication of the 1976 Task Force report some physicians reacted negatively to the proposal to inform women of their degree of risk. The Task Force believes that most of the criticisms were due to misunderstanding of the risk concept. The risk concept is not new. It is well known that disease patterns vary according to the distribution of risk factors within a population. In the Federal task force report dealing with the periodic health examination[34] risk factors were used to determine the usefulness of screening, as well as the optimum examination frequency, for a variety of conditions and diseases.

The reconvened Task Force reinforces the view that, based on epidemiological and sociological evidence, the female population can be classified into two different groups in terms of risk for cervical cancer:

a) the group *not at risk*, which should not be included in a screening program. This group comprises:

i) women who have never had sexual intercourse;
ii) women over age 60 who have been screened in the past and have been continuously negative (a woman over 60 who has been sexually active but has never been screened should enter the screening program);
iii) women who have had a hysterectomy for benign disease with adequate documentation that there has been complete removal of the cervical epithelium.

b) the group *at risk* for cancer of the cervix, which comprises all other women.

The 1976 report identified a high risk sub-group comprising women with early onset of sexual activity and women who have had multiple sexual partners. This subgroup probably also includes women whose husbands or other regular or only sexual partners have had multiple sexual partners. The question has been raised as to how in clinical practice women at high risk can be identified. The reconvened Task Force believes that information on degree of risk for cancer of the cervix should be generally available and should, for example, be available in physician's offices so that women who present with what appear to be more pressing medical or social problems can avail themselves of the opportunity to be screened, especially if they have never had a cervical smear. Special attempts should continue to be made to screen women who are attending clinics for sexually transmitted diseases or who are admitted to penal institutions.

As pointed out by Hakama et al[35] in order to justify concentrating on high risk women in a population screening program, the discrimination between low and high risk for cervical cancer must be greater than that implied by current knowledge of cervical cancer epidemiology. Furthermore, no data are available which indicate that women at high risk have a more rapid rate of progression from dysplasia or carcinoma in situ to invasive cancer (and death) than women who develop the disease in spite of being categorised as not at high risk. Hence selective screening based on the "high risk"/"at risk" distinction has only a limited applicability.

There is a further practical point that applies in Canada today. Because it has becomes increasingly common for women and men to have more than one sexual partner, many women born after 1945 will probably fall in the high risk sub-group as defined by the 1976 Task Force. It is reasonable that policies regarding ages at onset of screening and frequency of re-screening applicable to such women be recommended for all at risk women, without sub-categorization by degree of risk. Our knowledge of natural history suggests that most women born prior to 1955 who are going to develop cancer of the cervix should have already developed a detectable abnormality. This is especially true of those born before 1950. All at risk women in Canada born before 1955 should have already entered a screening program. If not they should be screened as soon as possible. The frequency of re-screening can then be dictated by the findings on the smear, rather than by their perceived degree of risk.

There is a yet no evidence that oral contraceptives of themselves increase the risk of developing cervical cancer.

It cannot be emphasized too strongly that women in whom dysplasia or carcinoma in situ is found must be removed from the *screening* program, and managed according to the severity of the lesion.

Chapter VI: Mathematical models of cancer screening

In the context of cancer screening mathematical models can be used in three ways. Firstly, they can be used to describe, in numerical terms, the impact of a particular disease in a defined population, assuming that all those affected by the disease are diagnosed and treated after the development of symptoms. With a slight abuse of language this would be designated as modelling the "natural history" of the disease. Secondly, models can be used to quantify the effect of screening (i.e. detection of the disease or its precursors in asymptomatic individuals) on the "natural history". Thirdly, using some criterion of desired effect, models can be used to determine optimal screening schedules.

All mathematical models of real world processes are simplifications, often gross over-simplifications. Greater realism can be obtained only at the expense of increased complexity, and this leads to two kinds of difficulties. The first is that the mathematical analysis becomes more tortuous and solutions in terms of formal mathematical functions may become impossible. To some extent this problem can be overcome by using computers to perform the calculations. A second difficulty with complex models results from the increased number of parameters to be estimated and the resulting requirement for data. This problem cannot be solved by bigger and better computers, and highly complex models are therefore only apparently more realistic.

Models are tautologies.* The structure and dynamic relationships are taken as given and the ensuing results are logical deductions from the basic assumptions. There is nothing in the results which is not implicit in the model. In practice the structure and parameters of the model are manipulated to fit known aspects of the real world (data), and the model is then pushed further to predict changes. Since many different models can be consistent with any set of data the predictions from any one model will not be actually observed in the real world.

Mathematical models are often encountered in biology and medicine under the heading of "compartment analysis".[36] Individual molecules are assumed to pass between different compartments in the body after introduction into one compartment. Within each compartment continuous mixing is assumed and fixed proportions of total content of each compartment are transferred to other compartments in any given instant of time.

A similar approach can be used to model disease processes, the compartments corresponding to various stages of the disease ranging from "healthy" to "dead". Individuals pass from one stage to another at fixed transition rates which, together with the initial numbers in each stage, determine the subsequent changes in these numbers. Such a model is *deterministic*, in the sense that fixed proportions leave each compartment per unit time. A more general, stochastic, version of the model would take into account chance variation in the numbers of transitions. *Stochastic* models thus provide probability distributions for the numbers of individuals in each stage, as well as the expected or the average numbers. In practice most users of the stochastic models restrict themselves to the expected numbers. Since it can be shown that, under very general conditions, the results of using the stochastic model for predicting expected numbers are the same as the results of using the corresponding deterministic model, the distinction is often semantic.

The simplest model of screening envisages a single pre-symptomatic stage during which the disease can be detected by some form of screening test, followed by definitive diagnostic procedures. In the absence of screening the pre-symptomatic stage would end in the development of symptoms, leading to diagnosis in the usual way. It is assumed (though the assumption must be verified empirically in each case) that the prognosis is improved by pre-empting the usual pattern and bringing the patient for treatment earlier. The difference between the time at which the patient is treated after detection by screening and the time at which she would have been treated in the usual way is called the lead time. Obviously it is not possible to determine the lead time directly, and the problem of estimating it indirectly from statistics on the incidence and prevalence of disease has received a good deal of attention.[37,38]

Let us suppose that a particular population is screened of all diseased individuals at some point in time and that the screening is repeated after, say, five years. During this interval some individuals enter the pre-symptomatic stage of disease. Those individuals who are still in the pre-symptomatic stage at the end of the five year interval will be detected by the next screen. Those who progress to develop symptoms before the end of the five year period may be detected as a result of their symptoms and will then not appear as detected by the screening net. It is assumed here that the screening procedure is perfectly sensitive and that mortality and emigration during the pre-symptomatic stage can be ignored. With these simple assumptions the proportion of new cases that would be detected during the screening interval is easy to derive mathematically. The model is analagous to a queue with an infinite number of servers, new customers arriving at random, and the time taken to provide ser-

*Oxford English Dictionary. Tautology — "The repetition of the same idea or statement in other words."

vice terminating at random.[39] By reducing the screening interval it is possible to make the proportion of cases detected by the screen as large as one pleases. Fig. 6 shows, for various average durations of the pre-symptomatic stage, the proportion of cases that would be expected to be detected with various screening intervals. For cancer of the cervix estimates of the mean length of the pre-symptomatic phase vary between 5 and 20 years, for which the screening interval required to detect 90 per cent of cases lies between 1 and 4 years.

There are several reasons why the theoretical estimates in Fig. 6 may not hold in practice. First, they are based on an extremely simple assumption about the distribution of the duration of stay in the pre-symptomatic stage. In particular this grants the possibility of extremely short and extremely long sojourns, which may or may not be realistic. The second oversimplification is the assumption that the screening test is perfectly sensitive, i.e. that there are no false negatives. Fig. 7 shows, for a mean pre-symptomatic stage of 10 years, the effect of increasing the proportion of false negatives from zero to 40 per cent. The reduction in the proportion of cases detected is more marked for longer screening intervals. A general stochastic treatment of the proportion of cases missed or detected has been given by Prorok.[40,41]

When we try to use this approach to develop recommendations for life-time screening schedules the model proves oversimplified in two other respects. First, the incidence of pre-symptomatic disease is not constant throughout a woman's lifetime. Second, women with pre-symptomatic disease are subject to general mortality which reduces the numbers who would, in the absence of screening, develop symptomatic disease. These deficiencies can be remedied by portioning the life-span into, say, five-year intervals and incorporating into the model age-specified incidence rates for pre-symptomatic cancer and for mortality from general causes. This approach has been used by several authors.[16,42,43] When applied to the case of screening for cancer of the cervix, where the pre-symptomatic stage of the disease usually begins in the third decade of life, the results, in terms of proportion of cases detected do not differ materially from the predictions of the simple model shown in Fig. 6.

Three general results emerge from the application of these models to a homogeneous (carcinoma in situ) experienced in established screening programs and to current female mortality rates*. First, about three-quarters of cases are detected by screening as infrequently as once in 10 years. Second, in order to virtually obliterate invasive disease it is necessary to screen more frequently than once in five years. Third, as screening is intensified the age of peak incidence of invasive disease falls. This is because most pre-symptomatic disease starts early in life. As the interval between screens is reduced only those cases with a short duration in the pre-symptomatic stage (i.e. those who progress to symptomatic disease at younger ages) are missed by the screening program.

A more direct measure of the benefit from screening is reduction in mortality or the potential years of life saved. Yu, Miller and Sherman[44] have used the general model of Knox[16] to investigate the effects of a variety of screening schedules on mortality, using Canadian statistics on incidence and mortality. Some of the results of their analyses are shown in Table III. Their conclusions on screening the at risk woman may be summarised as follows. As screening intensity increases, the yield from additional tests decreases. A mortality reduction of 90% or more follows nine or ten tests applied at appropriate ages. The appropriate age to initiate screening is 25 and nothing is gained by a repeat examination after one year unless the first smear is taken later than age 27. Up to age 40, three-yearly examinations are appropriate. From ages 40 to 60, five-yearly examinations will suffice. Screening examinations need not be continued after the age of 60 in women who have been previously screened and in whom no significant atypia was found. If a screening examination is missed on a three-yearly schedule, the woman should be called in for examination as soon as possible. If population acceptance falls below 80% every endeavour should be made to correct it. This is more effective than more frequent screening at a lower acceptance level. If the sensitivity of the screening test falls below 75%, it is more effective to rectify this than to attempt to compensate by screening more frequently.

*Three studies referred to in this section[42,44,49] are based upon data obtained from the British Columbia Cohort Study.[17]

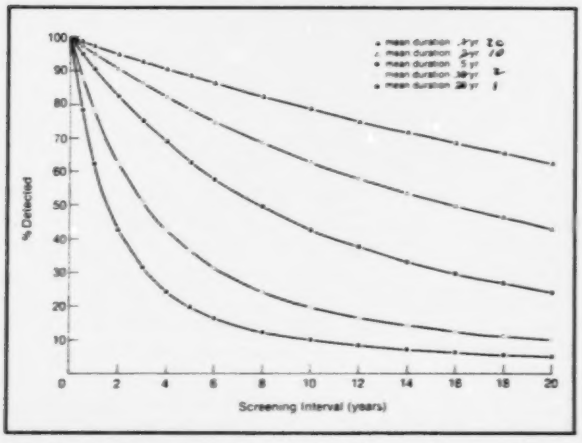

FIG. 6. — Proportion of cases detected according to estimates of mean duration of the pre-symptomatic stage of cancer of the cervix.

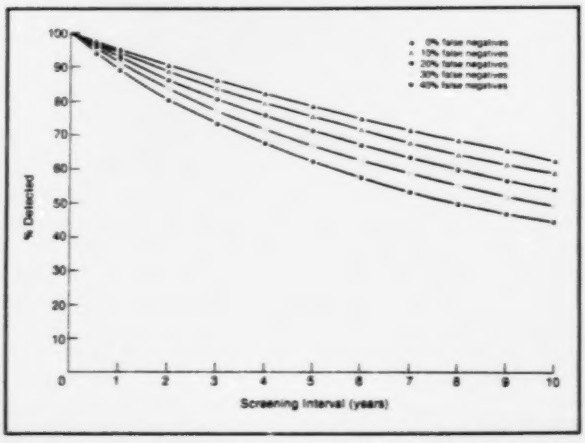

FIG. 7. — Proportion of cases detected according to various estimates of false negative proportions assuming a mean duration of pre-symptomatic stage of cancer of the cervix of 10 years.

When a younger and more progressive natural history was used for the simulations (an attempt to model a higher risk sub-group) some of the conclusions changed. The optimal age for starting screening is 20. Although a screening frequency of three-yearly examinations to age 35 and five-yearly to age 60 produces a satisfactory reduction in mortality, annual examinations to the age of 35 will yield additional worthwhile benefits.[44]

It is relevant that in an analysis of the duration of protection provided by a negative cervical cytology examination using data derived from the study of Clarke and Anderson,[22] it was found that maximum protection is provided by a negative smear for one year, somewhat less for negative smears after one to five years, and little or none after five years.[45]

A major application of screening models is to provide a basis for economic decision-making using cost-benefit or cost-effectiveness analysis. In cost-benefit analysis all the resources devoted to screening and all the effects of screening, including increased expectation of life, must be expressed in terms of dollars. It is difficult to get people to accept this approach, but if it could be done there would be theoretical advantages from the point of view of optimal allocation of resources both between and within programs. If each program is implemented at the point where the marginal *net* benefit is zero, resource allocation will be optimal over the whole system.

The cost-benefit approach has been used by Galliher,[42] who determined the net discounted costs per capita of various life-time screening schedules, the costs including screening costs, costs of treatment and the economic loss associated with premature death. Galliher concluded that the total cost is minimized when about ten cervical smears are taken during a lifetime, reducing to about five smears if the objective is simply to minimize medical expenses.

If the view is taken that it is not possible to put a dollar value on human life then cost-benefit analysis is not possible. An alternative approach which is frequently used in health applications is cost-effectiveness analysis. In this approach a particular beneficial effect of the program is selected (e.g. increased expectation of life) and the ratios of this benefit to the dollar costs of various programs are compared. This approach can be used to allocate resources to different programs either on the basis of average cost per unit benefit, or on the basis of marginal costs, which is preferable.[46] The method is less useful for determining the optimal level of activity within a particular program since there is no theoretical cut-off point equivalent to the point of zero marginal *net* benefit as in cost-benefit analysis.

The cost-effectiveness approach has been used extensively by Eddy[43] and the results have been used as the basis of revised recommendations on health examinations by the American Cancer Society.[47] Eddy presents diagrams of the cost-effectiveness of cervical cancer screening frequencies of one to five years beginning at age 25 for women at average risk and women at twice the average risk. For average risk women life expectancy is increased by 54 days with five-yearly screening, and this benefit increases to 67 days with annual screening. The discounted program cost increased from 55 dollars per woman with five-yearly screening to 313 dollars with annual screening. Both the average and marginal cost of increasing life expectancy rise sharply as screening frequency increases. Eddy also gives estimates of the decrease in lost earnings resulting from screening. Using this criterion a cost-benefit analysis is possible and the net benefit is maximized with four-yearly screening for the average risk woman. For a woman at twice the average risk, screening every three years is required to minimize the cost-benefit difference.

The cost-effectiveness approach has also been used by Schweitzer and Luce.[48] These authors restricted their attention to women aged 30-39 years and used a model incorporating dysplasia as well as carcinoma in situ and invasive carcinoma to estimate the marginal lives saved and marginal cost of screening at intervals of 10, 9, . . . 2, 1 years. The additional cost per additional year of life saved increased from $ 160, for a change from 10-yearly to 9-yearly, to $ 1,590 for a change from 2-yearly to yearly. Schweitzer and Luce restricted their analysis to comparison of marginal cost-benefit ratios leaving the reader to decide on an appropriate cut-off point. However, if the factor for lost earnings used by Eddy is applied to the results of Schweitzer and Luce, a five-yearly interval minimizes the cost-benefit difference.

The models and approaches discussed so far are applicable to the case of a physician planning the screening schedule for an individual woman, or to the actuarial determination of the premium required over time for an individual woman entering a screening program. The perspective of a public health official trying to optimize resource allocation for screening a total population is different. An approach which deals directly with the public health perspective is that of Albert, Gertman, Louis and Liu.[49] These authors have developed a completely general stochastic model of screening for cancer and other chronic diseases. For any individual the lengths of stay in each stage are treated as random variables. In their

Table III—Summary of results of computer simulation of screening programs†

Screening schedule			Total no. of tests per lifetime	Mortality per 10 000 women born	Percentage reduction in mortality
Onset age (yr)	Frequency	End age (yr)			
"At risk" women					
None			0	108.3	-
20	3, 5 yearly*	55	8	9.4	91
25	3, 5 yearly*	60	10	7.1	93
22	3, 5 yearly*	65	12	6.4	94
20	3, 5 yearly**	60	11	7.8	93
25	3 yearly	58	12	5.4	95
25	1, 2 yearly***	61	22	1.7	98
"High risk" women					
None			0	132.7	-
25	3, 5 yearly*	60	10	28.6	78
20	3, 5 yearly**	60	11	11.0	92
20	3, yearly	53	12	9.2	93
25	1, 5 yearly**	60	16	3.1	98
20	1, 5 yearly**	60	21	1.3	98
20	1, 3 yearly**	60	24	1.1	99

*Change frequency at age 40.
**Change frequency at age 35.
***Change frequency at age 31.
†Based on findings of Yu, Miller and Sherman[44].

application of this model to cervical cancer screening Albert et al use three disease states — carcinoma in situ with or without microscopic invasion, occult invasive cancer, and frankly invasive cancer. The effects of screening at various frequencies between ages 35-84 ("uniform" screening) are compared with the effects of "adaptive" programs in which the age distributions in each stage are examined annually and those age-groups with the highest proportion of detectable pre-symptomatic cases are given preference in the next year. The authors conclude that the so-called adaptive policy is more efficient in terms of the ratio of cases of pre-symptomatic disease detected to number of cases screened. The age-groups selected change from year to year whatever the intensity of screening. In terms of the cumulative yield of detected cases the authors found little to be gained by adaptive screening at a high intensity (four times in five years) compared with medium intensity (once every two years).

It is difficult to summarize the results of the various models of cancer screening, since they differ so much in the assumptions made and the criteria used to determine optimality. However, some general conclusions are possible.

- First, the models confirm what is intuitively obvious, namely that there are diminishing returns to increasing the frequency of screening in a given cohort of women.

- Second, it follows from the situation of diminishing returns that, from the public health point of view, it is better to spend money on increasing initial recruitment than on increasing the frequency of screening for those already screened.

- Third, and again from the public health perspective, an adaptive policy in which screening is done on the basis of the current screening history of the target population is more beneficial than prescribing a life-time schedule for all women. Obviously, this advantage can be gained only if screening programs are organized on a community basis.

- Fourth, measures to improve the quality and sensitivity of screening programs will be more effective in reducing mortality than will increasing the frequency of screening.

Chapter VII: Screening schedules

The 1976 report recommended that a woman should enter a screening program when she became sexually active or at the age of 18, whichever was later; should have a repeat smear at an interval of one year; three-yearly smears to age 35; and five-yearly smears thereafter to age 60, always providing that the smears were satisfactory and without significant atypia.

This proved to be one of the most controversial of all the recommendations.[50] A point which most commentators missed was that it was the intention of the Task Force that the recommendations be taken as a whole. It was not intended that policies of screening frequency less than the previously recommended annual examination should be established in the absence of registries of all screening examinations (in a clinic or region or province) which would monitor the frequency of screening in individual women and ensure that invitations for attendance for re-examinations were issued at appropriate intervals. Nor was it intended that screening frequency be reduced without reliable and satisfactory quality control measures. Further comments on quality control and registries appear in Chapters IX and X. In this section the Task Force considers again the questions of age of onset of screening, frequency of rescreening, and age of cessation of screening — all on the assumption that mechanisms *will* be in place to ensure that women are reminded to have examinations at the appropriate time.

In the Nordic countries, mass screening programs have been introduced on a four or five-yearly basis. In Britain the recommendation of the Ministry of Health is to initiate screening at the age of 35, and to continue at five-year intervals to the age of 70, as a minimum. Spriggs and Husain,[51] on behalf of the British Society of Cytology, recommended initial screening at the age of 25 if resources permit, and that rescreening should be initially five-yearly, then three-yearly from the age of 35. These recommendations were based largely on the computer simulations of Knox.[52] Miller, [21] in contrasting the recommendations of Spriggs and Husain[51] with those of the 1976 Task Force report, pointed out that they were based on a different interpretation of natural history and on different weights applied to deaths at younger ages. Further, the British recommendations were directed to achieving the greatest impact on a largely unscreened population, whereas the Task Force's recommendations were directed to achieving the maximum benefit with the most efficient use of resources in a country with established screening programs. However, it is relevant that McGregor and Teper,[53] on the basis of their experience of the screened population in Aberdeen, also recommend that screening should not be offered to woman under the age of 25.

In the United States, the American Cancer Society[47] has recommended three-yearly screening for at risk women starting after the onset of sexual activity. These recommendations were largely based on a mathematical model developed by Eddy.[54] The 1976 Task Force report was also quoted as evidence in favour of the change. The American Cancer Society's recommendations possibly created even more controversy in the United States than the 1976 Task Force report did in Canada. A statement criticising the recommendations defended annual cervical smears on the grounds that they brought women for other gynecologic examinations, including breast examinations. The difficulty of identifying high risk women and the problems of sample preparation and quality control in laboratories were also cited as reasons for carrying out an annual smear.[55] Similar statements were prepared by the American Society of Cytology and the American Society of Obstetricians and Gynecologists. These issues were debated extensively in the NIH Consensus Development Conference on Screening for Cancer of the Cervix. The report of the panel[56] recommended a one to three year frequency, presumably depending on the assessment by a womam's physician of her degree of risk and his assessment of the available evidence on frequency. However, it was accompanied by a minority report by Neuhauser, who argued for a reduced frequency on economic grounds.

In Canada, there is some evidence that physicians have not yet accepted the 1976 recommendations on frequency.[2] Nevertheless, the recommendations are being incorporated in the training of physicians, and more extensive impact can be expected in future.

For this report the 1982 Task Force has approached the re-examination of optimum screening schedules largely from an assessment of mathematical models (see Chapter VI) and particularly through the application of inferences on natural history derived from the British Columbia Cohort Study,[17] and recent Canadian trends in incidence and mortality, to the Model of Knox.[16] Full details of these simulations are given by Yu, Miller and Sherman.[44] Some of the results of their analysis are shown in Table III, in Chapter VI, which also includes a summary of their conclusions.

It has been pointed out by others (e.g. Galliher[42]) that as the number of cervical smears done in each woman's lifetime increases the additional benefit becomes less and less. Lacking any valid method to adequately distinguish those women destined to develop and die from invasive

cancer of the cervix from those who will develop curable invasive cancer or never develop the disease, it becomes a matter of judgement, to which the public as well as medical scientists should contribute, how much in the way of resources should be invested in screening programs.

It is the opinion of the Task Force that screening programs should aim at preventing at least 90% of mortality from cancer of the cervix that would occur in the absence of screening. The Task Force has not attempted a detailed cost-effectiveness analysis. Previous approaches to such analyses have shown that most of the costs come from the application of the screening test and, therefore, that the cost is largely a reflection of the numbers of tests done. Furthermore, applying dollar costs in a cost-effectiveness analysis implies greater precision than the data and the resulting simulations justify. The Task Force has also avoided cost-benefit analyses because it is difficult, if not impossible, to measure benefit precisely and because of reluctance to place a value on human life and suffering, even though this would be required to make an informed judgement on the resources to be applied to this or other health programs.

Given the difficulties (discussed in Chapter V) of identifying and classifying high risk women, the probability that many young women now have the high risk type of natural history modelled, and the desirability of providing consistent recommendations for all ages, the Task Force interprets the results from mathematical modelling as reinforcing the general validity of its previous recommendations. In general, Canadian women aged 35 years or more have now entered screening programs, and should require no more than five-yearly screening. Since younger women are sexually more active, and increasingly tend to have more than one partner, they are at high risk, and therefore annual screening is justifiable until age 35. The only specific changes proposed to the 1976 recommendations are therefore:

i) No attempt should be made to categorize women at high risk on a group basis.
ii) Women who have had sexual intercourse should generally be advised to have annual screening from the age of 18 until they reach 35.
iii) Women over the age of 35 who are assessed as being at continuing high risk, either by their contact with the health care system in VD clinics, by their presence in penal institutions, or by their own judgement or that of their physicians, should not be discouraged from having smears more frequently than every five years if they request them.

The following recommendation of the 1976 report still holds:

- Women over the age of 35 should, in general, be advised that they should be screened every five years.

It should again be emphasized that these recommendations on screening frequency over the age of 35 are based on the availability of an appropriate registry mechanism to maintain surveillance to ensure that the recommendations on frequency are not allowed to be translated into less frequent schedules by default. Further, they require the availability of physicians or others who know how to take adequate smears, and skilled cytology assessment in laboratories with adequate quality control programs. They also apply only to women who remain free from abnormal cytology indicating epithelial atypia. Whenever such changes are detected on a cervical smear, schedules of repeat examinations should be dictated by the requirements for surveillance, diagnosis, treatment and adequate follow-up of the abnormalities identified.

Chapter VIII: Cytologic screening coverage of the Canadian population

Table IV shows the cytologic screening coverage, in Canada and the provinces, of the female population aged 20 and over for the years 1971, 1975, 1977 and 1979. The data for 1971 were included in the 1976 report. The figures are based on the number of cytologic examinations performed in each province as reported in a recently completed survey by the Canadian Society of Cytology*.

It is apparent that in Quebec and the Atlantic Provinces there was a significant increase in the number of smear examinations performed up to the mid '70s with a more modest increase occurring in the other provinces. However, since then the increase in the number of smear examinations in Ontario, Manitoba, Saskatchewan, Alberta and British Columbia, has been in parallel with the increase in population, so that the number of examinations expressed as a proportion of the female population over age 20 has remained relatively constant. Elsewhere there has been a relatively slight increase, with an impression of stability from 1977 to 1979. Indeed, the proportions in 1979 show a remarkable uniformity across the country with the exception of the higher proportion still reported from British Columbia.

It should be noted that these figures are for smear examinations and do not necessarily represent the proportions of women examined. Increases might be due to re-examinations of the same women, without any increase in the proportion of the population covered by the screening programs. Only when it is possible to directly relate registers of smear examinations to population registers in the various provinces will it be possible to estimate the population coverage and, particularly, the proportion of the population that has never entered screening programs. In 1970 the proportion of cytologic examinations that were first examinations was 27% in British Columbia. By 1980 this figure had fallen to only 10%. Undoubtedly a similar trend will have occurred in those other provinces which have significantly increased the proportion of women who are being re-examined annually.

*In preparation.

Table IV—Extent of cervical screening, Canada and the provinces, 1971, 1975, 1977 and 1979*†

No. of screenings per 100 women aged 20 years or more*

Province	1971	1975	1977	1979
British Columbia	55	61	55	57
Alberta	40	48	47	48
Saskatchewan	41	47	48	47
Manitoba	46	51	50	48
Ontario	39	45	44	44
Quebec	29	42	43	45
New Brunswick	22	41	37	40
Nova Scotia	37	35	45	46
Prince Edward Island	28	37	41	44
Newfoundland	36	43	42	44
Canada	38	45	45	46

*Not to be equated with the number of women screened.
†Source: Unpublished data from the Canadian Society of Cytology, 1980 Survey.

Chapter IX: Quality control in cytologic screening programs

Since the publication of the 1976 Task Force report very little has been done in Canada regarding the formal development of specific quality control programs for cytology. However, in Ontario, the Laboratory Proficiency Testing Program, which began to function in the field of cytology in 1977, has documented some statistics for the period 1977-81, concerning diagnostic accuracy in cervical cytology. These statistics are presented in Table V. It is apparent that there was a significant lack of uniformity of diagnosis in the categories of dysplasia and malignancy in the results from the 160 participating laboratories. The findings have been made available to the participating laboratories, and appropriate educational programs have been initiated. It is hoped that these efforts will results in an improvement in performance.

The controversy regarding volume of cases in cytology laboratories has been confused because it was overlooked that the 1976 report had advocated a minimum volume of 25 000 cases per annum in cytologic laboratories for reasons of *efficiency* rather than *proficiency*. The data from the Ontario Proficiency Testing Program indicate that proficiency varies considerably between laboratories handling similar numbers of cases. No particular level of case load implies a monopoly on either good quality or poor quality in laboratory performance. However, these data are not relevant to the considerations of efficiency which were discussed more fully in the 1976 report.

There are several links in the chain of good quality screening and it is pertinent to highlight the many possible reasons for a 'false negative' result from a given cervical smear.

A. Possible causes of 'false negative' reports in cervical-vaginal cytology

1. Error in documentation of smear
   a) in the physician's office or in the clinic
   b) in the processing of smears in the laboratory
   c) in the report issued to the clinician

2. Inadequate or improper sampling of a lesion
   a) choice of sampling techniques not appropriate for the end result desired
   b) insufficient cellular material in the samp'e
   c) poor technique in spreading sample (too thick, ridged, etc.)
   d) transformation zone not well represented in sample
   e) lesion not amenable to adequate sampling:
      i) extremely small in size
      ii) located high in endocervix or in outer endocervix or vaginal vault
      iii) highly keratinized variant (pertinent cells not apparent at surface)
      iv) surface of lesion altered by necrosis, ulceration, bleeding secondary infection, etc.
      v) possible physiologic or biologic variation in desquamation of pertinent cells

3. Presence of interfering substances
   a) cellular material obscured by blood or menstrual debris

Table V–Data from Ontario Laboratory Proficiency Testing Program for gynecologic cytology, 1977-81*

	No. of laboratory diagnoses reported on test slides									% of laboratory diagnoses that deviated significantly†		
	Degree of deviation from committee diagnosis											
	Undercall				Overcall							
Committee diagnosis	≥3	2	1	0	1	2	≥3	No diagnosis reported	Total	Undercall	Overcall	Total
No abnormal cells	NA	NA	34	511	112	12	4	4	677	NA	2.4	2.4
Benign atypia	NA	NA	173	913	96	11	4	5	1202	NA	1.2	1.2
Mild dysplasia	NA	39	119	133	27	1	1	2	322	12.1	0.6	12.7
Moderate dysplasia	8	58	98	102	48	25	NA	1	339	19.5	7.7	27.2
Severe dysplasia	31	27	57	54	52	5	NA	0	226	25.7	2.2	27.9
Malignant squamous cells	58	35	91	300	14‡	NA	NA	0	498	18.3	NA	18.3

*Testing was carried out by circulation of eleven test slides to all 160 laboratories processing gynecologic cytology specimens. These data are aggregated from the first four complete surveys. No = not applicable.
†More at least two degrees different from the committee diagnosis.
‡An additional type of malignant abnormality was recorded by the laboratory but not categorized as such by the committee (e.g., sarcoma cells in addition to malignant squamous cells).

b) cellular material obscured by surface bleeding
c) cellular material obscured by lubricant
d) cellular material obscured by excessive inflammatory exudate
e) cellular material obscured by talcum powder granules
f) cellular detail altered by cytologic bacterial action

4. Technical problems in processing

a) inadequate fixation of smears

i) air drying
ii) incomplete fixation

b) overstaining, understaining, improper mounting etc.

5. Errors in screening and reporting

a) inadequate (incomplete) screening of slide (careless or inattentive screening)
b) misinterpretation of cellular abnormalities (under-categorization)

i) inadequate training and/or experience
ii) inadequate supervision and quality control

B. The 'adequate' cervico-vaginal smear

Over the past 20 years there have been many controversies concerning a) the most satisfactory technique for sampling the cervix; and b) the criteria by which a cytologic sample may be categorized as adequate once it has been examined microscopically. Some of the reasons for a cervical smear being inadequate are obvious from the listing of the possible causes of a false negative smear. Even if these pitfalls are avoided there is still the possibility that a smear may not adequately reflect the cytopathology of a lesion which is present in the cervical epithelium. For example, it has been traditionally thought that the presence of some endocervical cells in an otherwise satisfactory cervical smear would confirm that the sample was adequate, the implication being that the presence of endocervical cells indicates that the upper margin of the transformation zone has been included in the sampling. However, in a number of cases a smear of the upper or endocervical area of a very broad transformation zone may not be the ideal sample. It is now well established that many cases of dysplasia, carcinoma in situ, and micro-invasive carcinoma, may be manifest primarily within that area of the transformation zone that is immediately adjacent to the original squamocolumnar junction.[57] This area and the adjacent broad transformation zone may be composed entirely of squamous epithelium at the time of detection of an abnormal lesion. The most representative direct sample in these cases may therefore contain no endocervical component. Conversely, the small-cell type of cervical malignancy is most commonly demonstrated near the junction of the endocervix with the active transformation zone of the cervix, and these lesions also may not be sampled in a cervical scrape from the lower portion of the transformation zone.

It is recognized that there are differing characteristics of lesions within the spectrum of cervical dysplasias and cancers, in regard to such features as cell type, location, locale of initiation of invasion, modification by keratinization, occurrence either within or separate from condylomatous lesions, overall extent, and tendency to be focal or multifocal. Recognizing these variables, and with the realization that much of the yield of screening activity in recent years has been cases of mild or moderate dysplasia, in which the abnormality is usually small or localized, it is important that the direct cervical sample should be circumferential. The sample should be adjusted when necessary to accommodate any variant of location of the original squamous columnar junction and the extent of the transformation zone that may be grossly evident, in order to ensure as adequate a sample as possible.

C. Reporting terminology

The 1976 Task Force report emphasized the need for more uniform terminology in the reporting of cervical cytologic specimens. The report included a recommended nomenclature. This nomenclature is reproduced below (Table VI) with two important additions to the category "abnormal cells consistent with benign atypia (non-dysplastic)" which have resulted from advances in our understanding of cytologic abnormalities over the past few years. These additions are "atypical metaplasia" and "condyloma effect."

Squamous metaplasia, in its usual form without recognizable atypia, is an extremely common finding in the active typical transformation zone of the cervix and is now usually recorded as a finding to be noted within the category of "no abnormal cells." However, cells consistent with squamous metaplasia but with some

Table VI—Reporting terminology for cervical – vaginal cytology

- **Unsatisfactory (reason to be stated)**
- **No abnormal cells**
  - **Metaplasia noted**
- **Abnormal cells consistent with benign atypia (non-dysplastic)**
  - **Inflammatory effect**
  - **Trichomonas effect**
  - **Viral effect**
  - **Yeast effect**
  - **Irradiation effect**
  - **Keratinization**
  - **Atypical metaplasia**
  - **Condyloma effect**
  - **Other**
- **Abnormal cells consistent with dysplasia***
  - **Mild dysplasia**
  - **Moderate dysplasia**
  - **Severe dysplasia**
- **Abnormal cells consistent with malignancy**
  - **Consistent with in situ squamous carcinoma**
  - **Consistent with invasive squamous carcinoma**
  - **Consistent with adenocarcinoma**
  - **Type unspecified**
- **Abnormal cells not specifically classified**
  - **(comments to be attached)**

*See discussion of C.I.N. terminology in the text.

added cellular atypia may be categorized as "atypical metaplasia".

In recent years there has been considerable controversy concerning condyloma acuminatum.[58,59,60,61,62] Further clarification, particularly of the relationship of condyloma acuminatum to dysplasia or malignancy, will probably occur in the next few years. It is recommended that "condyloma effect" be specifically noted.

Under the category of "other", in the group of benign atypical abnormalities, the cellular findings associated with chlamydia trachomatis are now being more frequently reported in many areas of North America,[63,64] as are also fungal organisms consistent with an Actinomyces infection,[65] which is found particularly in women with intrauterine contraceptive devices.

C.I.N. terminology

An alternative terminology known as the cervical intraepithelial neoplasia, or C.I.N. terminology, has been employed for several years by many laboratories and clinicians. C.I.N. has been used as a broad term to encompass the spectrum of lesions that many other laboratories and clinicians prefer to designate more specifically in the categories of mild dysplasia, moderate dysplasia, severe dysplasia and carcinoma in situ of cervical squamous epithelium.

Several microscopic features and other types of evidence express a strong inter-relationship between dysplasia and carcinoma in situ, and the bordeline between severe dysplasia and carcinoma in situ is somewhat arbitrary or subjective. Nevertheless, the various categories of dysplasia differ significantly in degree of microscopic abnormality. Also features such as the persistence of the lesion, the possibility of regression, the rates of progression or conversion to more advanced abnormality, the extent of the lesion, and the most appropriate or rational therapy can differ substantially within this group of categories. In using the C.I.N. terminology, therefore, a subdivision into separate categories is required, with the categories usually designated by number:

- C.I.N. (i) — corresponding to "mild dysplasia"
- C.I.N. (ii) — corresponding to "moderate dysplasia"
- C.I.N. (iii) — corresponding to "severe dysplasia to carcinoma in situ".

The hazards and limitation inherent in the use of numbers to denote abnormalities in cytologic reporting have been recognized for many years.

Unfortunately the term "neoplasia" as it is used in a specific sense in pathology may be broadened to include "pre-neoplasia". When too loosely applied a term such as "intra-epithelial neoplasia", with its built-in lack of specificity, is prone to indiscriminate use and may include a cytologically, histologically and clinically ill-defined mixture of lesions.

In the opinion of the Task Force, the C.I.N. terminology has compounded the difficulty in the correlation and reproducibility of data from various screening programs, treatment clinics and registries regarding the incidence, treatment and follow-up analysis of preinvasive lesions of the cervix. For these reasons this terminology is not recommended and has not been used in this report.

Chapter X: Population registries for cervical cytology screening programs

In the 1976 report, the Task Force Force recommended that "provincial registries should be established to record data and to carry out recommendations VI (a) and VI (c)". **Recommendation VI (a) was as follows:**

That normal patients are recalled at regular intervals for repeat smears according to the guidelines of the program.

Recommendation VI (c) was:

That long-term follow-up be provided for patients who have received treatment following the diagnosis of an abnormality.

The Task Force also recommended:

Such a system can only be effected through a centralized registry. In Canada, provincial registries should establish uniform data-processing systems so that inter-provincial communication and comparisons will be possible.

It is perhaps an indication of the failure of those who considered the 1976 recommendations to recognize that they were an integral and complete package, and that the recommendations on frequency should not be considered in isolation, that only Nova Scotia has established a provincial registry since the 1976 report, and that even this was being planned at the time that report appeared. In Quebec, two large laboratories (one in Montreal and one in Quebec City) have established registries, but they do not together cover the total population of the province and they do not have the resources to carry out all the other recommendations. In Manitoba, an existing provincial cytology register (but which was not carrying out the functions intended by the Task Force) has even been abolished since 1976.[2]

As with all preventive medicine programs, it is necessary to consider who is responsible for ensuring that women enter cervical screening programs and, once in, continue to have cervical smears taken at the recommended intervals. In the opinion of the 1982 Task Force primary responsibility lies with the individual woman. Physicians, other health professionals, and government public health agencies have a role to play in education, so that all women can inform themselves of the recommended frequencies for having smears. Primary care physicians with stable practices may set up reminder mechanisms for their female patients who fail to return for smears. However, given the fallibility of human memory, and the mobility of the Canadian population, the Task Force believes that government sponsored registries are essential if the full potential of cervical smear programs is to be realized. All cervical smears would be recorded. So long as they were being done no less frequently than recommended, the registry would be "silent". However, whenever a woman went for longer than the prescribed interval without a smear the registry would issue a reminder to the patient.

Although issuing reminders for routine re-examinations is not necessarily an appropriate function of a physician's office, because of the mobility of the Canadian population, it should be noted that such reminders are routinely issued by dentists. It has been suggested that the regulations of the provincial licensing bodies in some provinces are interpreted to mean that physicians are not permitted to invite women to return for repeat smear examinations if previous smears were negative. The Task Force recommends:

- That provincial licensing bodies should ensure that their Medical Acts and Regulations are amended, if necessary, to permit physicians to remind their patients that the time has come for them to have a repeat cervical cytology examination, or indeed, any other recognized preventive medical procedure.

The Task Force has also had representations that provincial registries having the follow-up function envisaged would be expensive and difficult to run, and might be regarded as an invasion of privacy. The Task Force rejects such arguments. Modern computer technology enables such registries to be run economically and has already been used elsewhere to ensure adequate compliance with immunisation schedules in children.[66]

It is not for the Task Force to determine how a cytology registry might be established in any province. This will depend on existing resources and personnel. Possible options include linking registries with provincial or regional cytology laboratories, with provincial cancer registries, or with the existing record systems of provincial medical insurance schemes. However, the previous recommendations should not again be allowed to go by default. The Task Force therefore recommends:

- That Departments and Ministries of Health should consult with the appropriate bodies in their jurisdictions (Director of the Provincial Cancer Control Agency, Director of the Provincial Cancer Registry, Director of the Medical Insurance Plans, Director of Provincial or Regional Laboratories for Cervical Cytology, etc.) with a view to selecting the best mechanisms to establish functional provincial registries of all cervical cytology examinations as soon as possible.

- That mechanisms which already exist in each pro-

vince to determine that young women are no longer regarded as dependents for health insurance purposes (usually at or about age 19) should be utilized as soon as possible to remind sexually active women that they should have a cervical smear if they have not already done so.

- That the Deputy Minister of National Health and Welfare should make available the resources of his Department to co-ordinate the establishment of provincial cervical cytology registries, to facilitate exchange of data, and to facilitate the transfer of records when women move from one province or region to another.

Chapter XI: Relationship to other screening programs

Several critics of the recommendations on frequency of screening which were made in the 1976 Task Force report felt that whatever the merits of an annual cervical smear, it was important to encourage women to see their physicians at least once a year in order that they could be examined for the presence of other conditions.

The Task Force had addressed itself to this issue. It had pointed out that the most common malignant diseases which affect women in Canada — cancer of the breast, large bowel, ovary, lung and endometrium — occur in women 20-30 years older than those on whom a screening program for carcinoma of the cervix should concentrate. In addition, it was pointed out that the epidemiological characteristics of these conditions are quite different from those of women who are at highest risk of developing carcinoma of the cervix and that screening programs should be directed at appropriate "at risk" groups.

A particular and oft repeated criticism of the Task Force's recommendations has been that women should have annual pelvic examinations and that to perform such an examination without taking a cervical smear at the same time is poor medical practice. One response to this criticism is to point out that cervical smears involve more expenditure of resources than just physicians' time. Cervical cytology demands high quality laboratory examination and means for transportation of specimens and reports. Unnecessary utilization of such resources cannot be supported. Cervical smears should not be taken primarily to detect such conditions as moniliasis and trichomoniasis. Even more important is to consider the justification for the annual examination itself. There is no evidence that the early detection of cancer of the endometrium or of the ovary in asymptomatic women is facilitated by such examinations. None was available at the time of the 1976 report and none has appeared since.

In order to justify searching for a condition in a screening program, several criteria must be met. There must be a practical and cost-effective method of detecting the condition in the pre-symptomatic stage, there must be an effective treatment, and there must be evidence that treatment during the pre-symptomatic stage will improve the natural history of the condition to a greater degree than treatment started after the patient has developed symptoms.[67]

Since publications of the 1976 Task Force report another Task Force has reported on all aspects of the periodic health examination.[34] In a comprehensive review, the Task Force on the Periodic Health Examination made recommendations regarding frequency of application of detection manoeuvres at particular ages. There was only one manoeuvre for which the quality of evidence was judged "good", having been derived from a randomized controlled trial, which the Task Force on the Periodic Health Examination felt should be applied more frequently than this reconvened Task Force feels is necessary for screening for carcinoma of the cervix. This was mammography and physical examination of the breast, recommended annually from the age of 50 to 59. However, because the independent effect of mammography in this age group is uncertain, a further randomized trial has been initiated in Canada.[68] Thus action on this recommendation should be deferred pending results of this trial.

The frequency of cervical cytology screening should be determined on its own merits, not with a view to conducting an annual examination for some other purpose. Women should be invited to have the other screening tests on *their* merits; a cevical smear which is not required at that particular time should not be done incidentally to other tests. It goes without saying, however, that when more than one screening examination is indicated in a particular age span, they should be coordinated with each other and with other necessary visits to the physician's office or public health clinic.

Chapter XII: Management of patients with abnormal cervical smears

In the 1976 report of the Task Force on Cervical Screening Programs the "usual investigation and treatment of carcinoma of the cervix" was outlined and the developing role of colposcopy in the evaluation of patients with abnormal cervical cytology was mentioned. Since then the role of colposcopy has become more clearly defined. In this section the 1982 "state-of-the-art" of the investigation of patients with abnormal cervical smears and the role of colposcopy in their assessment are described in general terms.

Cytological screening *detects* the presence of preclinical cervical dysplasia or neoplasia. Colposcopic examination *evaluates* the cervix with abnormal cytology and enables the colposcopist to select the site for biopsy for tissue diagnosis. Usually, this permits determination of the presence or absence of invasive cervical cancer.[69] Colposcopy is particularly valuable for assessing cervical abnormalities in young women. With an adequate biopsy it not only avoids the inherent morbidity and necessary hospitalization of cone biopsy, but also avoids the potential adverse effects of cone biopsies on future reproductive function.[70,71] Diagnostic cones can now be limited to those patients in whom colpscopic examination is unsatisfactory; to those in whom colposcopically directed biopsies have identified "microinvasion", in order to rule out more advanced disease; and to those who continue to show significant abnormal cytology the source of which cannot be identified colposcopically.[69,72,73]

Women with cervical cytology suggestive of moderate to marked dysplasia, of carcinoma in situ, or of invasive disease, should be assessed colposcopically. Women whose cervical cytology shows mild dysplasia should have the smear repeated at two or three month intervals; if the dysplasia persists they should be assessed by colposcopy. A diagnosis of significant dysplasia or carcinoma in situ in colposcopically directed biopsies is a frequent enough occurrence in patients with cytology reported as only mild dysplasia to justify such a policy.

There is not complete agreement between the various centres in Canada as to what constitutes proper management for patients with cervical dysplasia or carcinoma in situ. In general, patients found to have mild or moderate dysplasia by colposcopy and in whom the entire limits of the lesions have been identified, may be treated by conservative measures such as electrocautery or cryotherapy. Severe dysplasia and carcinoma in situ may be managed conservatively by cryo- or electrocautery in selected patients,[74,75] or by therapeutic conization or hysterectomy.[76] Treatment will depend upon the size and location of the lesion, the patient's age, parity and reliability for follow-up, and other medical and gynaecological considerations.

The diagnosis of microinvasive carcinoma following colposcopy requires a diagnostic cone biopsy to rule out more advanced disease. No standard pathological definition as to what constitutes microinvasive carcinoma (Stage Ia) exists among the various centres in Canada. However, a simple hysterectomy is generally considered to be adequate treatment.[77,78] Occult preclinical, invasive, carcinoma (Stage Ib) is treated either by irradiation or by radical hysterectomy and pelvic lymphadenectomy, depending upon the clinical findings, the age of the patient, and treatment policies in various centres.

From the foregoing it is clear that colposcopy offers a degree of flexibility in the evaluation and management of patients with preclinical cervical neoplasia that is not available with diagnostic conization. It is crucial, however, that early invasive carcinoma of the cervix not be missed by colposcopic assessment, since this would lead to inappropriate conservative therapy.[79,80] It must be stressed that colposcopy imposes a large degree of responsibility for accurate evaluation of the patient with abnormal cervical cytology on the colposcopist. For this reason the Task Force recommends that:

- Colposcopic examination should not be regarded as a screening technique, but as an important diagnostic tool for the localization and assessment of premalignant disease and early invasive carcinoma of the cervix in women with abnormal cervical smears.

- Colposcopic assessments should be performed only by those trained in gynaecology and with adequate training and experience in colposcopy.

- Colposcopists should work in clinical settings which will provide a continuing source of abnormal material, in order to maintain and enhance their expertise.

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